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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/341,600	09/15/1999	ALAN BERRY	3161-18-PUS	5327

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EXAMINER	
FRONDA, CHRISTIAN L	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 04/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/341,600	BERRY ET AL.	
	Examiner	Art Unit	
	Christian L. Fronda	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-76* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 September 1999* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/7/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 40-76 are under consideration in this Office Action.

2. The rejection of claims 40-70 under 35 U.S.C. 112, second paragraph, has been withdrawn in view of applicants' amendments filed 12/03/2004.

3. The rejection of claim 67 under 35 U.S.C. 102(b) has been withdrawn in view of applicants' amendment filed 12/03/2004.

4. The rejection of claims 40-70 under 35 USC 101 has been withdrawn in view of applicants' amendments and arguments filed 12/03/2004.

5. The rejection of claims 40-47, 51, 53-70 under the judicially created doctrine of obviousness-type double patenting has been withdrawn in view of applicants' filing a the terminal disclaimer. The terminal disclaimer filed on 12/03/2004 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. Patent No. 6,372,457 has been reviewed and is accepted. The terminal disclaimer has been recorded.

6. Claim 73 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 50. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claim 40-76 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants' arguments filed 12/03/2004 have been fully considered but they are not persuasive. Applicants' position is that since the claims are now limited to microorganisms that are genetically modified to overexpress glucosamine-6-phosphate synthase or have been genetically modified where the coding region of any gene encoding glucosamine-6-phosphate synthase is modified resulting in increased enzyme activity, the specification is fully enabling for such microorganisms. Applicants argue that the Declaration of Dr. Deng shows that any gene encoding glucosamine-6-phosphate synthase can be used in the claimed invention. Applicants argue that it is not necessary to have prior knowledge of the amino acid sequence of the claimed glucosamine-6-phosphate synthase or knowledge of where in the amino acid sequence the claimed mutations occur since applicants assert that the screening of 4368 transformants illustrated in Example 5 yielded six candidates that were found to be superior glucosamine producers. Applicants conclude that in view of Example 5, it is not unpredictable to produce and select mutants meeting the limitations of the claims. The examiner respectfully disagrees for reasons of record as supplemented below.

Until the specific mutations within the coding region of the gene encoding any glucosamine-6-phosphate synthase that accounts for an increase in enzyme activity or decrease in product inhibition, the specification simply extends an invitation to one skilled in the art to further do trial and error experimentation to arrive at the claimed glucosamine-6-phosphate synthase that has increased enzyme activity or decreased product inhibition. While the Declaration of Dr. Deng shows that wild-type genes from other biological sources encoding glucosamine-6-phosphate synthase may be used in the claimed method, it does not teach how to make any microorganism comprising any genetic modification that increases glucosamine-6-phosphate synthase action or any genetic modification in the coding region of a nucleic acid sequence encoding glucosamine-6-phosphate synthase including deletion, insertion, substitution, or combinations thereof of specific nucleotide(s). Despite several amino acid residues which may be involved in catalysis, trial and error experimentation must be performed on the other amino acid residues to arrive at the at the claimed glucosamine-6-phosphate synthase that has increased enzyme activity or decreased product inhibition.

Example 5 shows a large amount of trial and error experimentation that is outside the realm of routine experimentation was required to identify only six candidates that are superior glucosamine producers. One of skill in the art cannot predict from the specification's illustration

of screening 4368 transformants in Example 5 that candidates could be found with increased enzyme activity without actually performing this large and extensive amount of searching and screening experimentation. The examiner takes the position that general teachings for screening and searching for the glucosamine-6-phosphate synthase with the desired properties is not guidance for making the claimed invention. Furthermore, such screening and searching for the glucosamine-6-phosphate synthase with the desired properties shown in Example 5 does not exclude experimentation using site-directed mutagenesis, for example, on the coding sequence of a polynucleotide encoding glucosamine-6-phosphate synthase to screen and search for the mutation that results in an enzyme having increased activity or decreased product inhibition.

The Examiner finds that one skilled in the art would require additional guidance, such as the specific type of genetic modification to perform on the specific codons within the coding region of any polynucleotide encoding glucosamine-6-phosphate synthase that lead to the desired increase in enzyme activity or decreased product inhibition. Without such a guidance, the experimentation left to those skilled in the art is undue.

9. Claims 40-76 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants' arguments filed 12/03/2004 have been fully considered but they are not persuasive. Applicants' position is that the specification provides sufficient guidance, combined with knowledge in the art at the time of the invention, to show that the inventors possessed the invention as claimed. Applicants argue that structural homology does not necessarily equate to overall sequence homology. Applicants argue that the examiner is incorrect in concluding that because the Declaration of Dr. Deng states a low overall homology of genes from other biological sources encoding glucosamine-6-phosphate synthase, then the *E.coli* gene encoding glucosamine-6-phosphate synthase is not representative of the claimed genus. The examiner respectfully disagrees for reasons of record as supplemented below.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definitions, such as the structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v, Eli Lilly and Co.* 43 USPQ2d 1398 (Fed. Cir. 1997), quoting *Fiers v. Revel,* 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe the genus of

genetic materials, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g. structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

The claims are genus claims that are directed toward any microorganism comprising any nucleic acid having any genetic modification that increases glucosamine-6-phosphate synthase activity or reduction of product inhibition of glucosamine-6-phosphate synthase activity, and the use of the claimed microorganism for the production of glucosamine. The scope of the claimed genus includes many microorganisms , many glucosamine-6-phosphate synthases of any structure and amino acid sequence from any biological source, and many genetic modifications to obtain the desired property. Furthermore, the genus is highly variable because a significant number of structural differences between genus members exits.

In order to meet the written description requirement, the specification must describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus. The Declaration of Dr. Deng clearly shows in Table 1 that glucosamine-6-phosphate synthase sequences from other biological sources including *B.subtilis, C.albicans, and S.cerevisiae* have low homology to *E.coli* glucosamine-6-phosphate synthase. Thus, the skilled artisan would not be able to predict the structure of other species encompassed by the claimed genus by the single description of the *E.coli* glucosamine-6-phosphate synthase. Furthermore, the references of Fernandez-Herrero et al., Leriche et al., Smith et al., and McKnight et al. cited by applicants do not teach that the amino acid sequence of the *E.coli* glucosamine-6-phosphate synthase is representative of the claimed genus nor do they teach how a skilled artisan can predict the structure of other species encompassed by the claimed genus from the *E.coli* glucosamine-6-phosphate synthase.

In view of the above considerations, applicants have failed to sufficiently describe the claimed genus, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Conclusion

10. No claim is allowed.

11. **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Friday between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

13. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CLF

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